EXPRESS MAIL NO.: EL 500 575 459 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Application of: Nehls *et al.*

Serial No.: 09/398,253 Art Unit: 1631

Filed: September 17, 1999 Examiner: Young J. Kim

For: NOVEL HUMAN POLYNUCLEOTIDES AND POLYPEPTIDES ENCODED THEREBY Docket No.: 8535-026-999

APPELLANTS' BRIEF ON APPEAL

Laura A. Coruzzi, Esq.
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

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#20/Appeal Brief

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APPELLANTS' BRIEF ON APPEAL UNDER 37 C.F.R. §§ 1.191 AND 1.192

Pursuant to the provisions of 37 C.F.R. §§ 1.191 and 1.192, an appeal is taken herein from the final rejection of claims 1, 3, 4, 10, and 11 of this application. Appellants submit an original and two copies of this appeal brief accompanied by: (1) a Petition for Extension of Time (in duplicate) for five months from March 3, 2002 up to and including August 3, 2002 (which falls on a Saturday), accompanied by the appropriate fee; and (2) a Brief on Appeal Fee Transmittal Sheet (in duplicate). Appellants also submit herewith Exhibit A: an appendix of the claims (*i.e.*, claims 1, 3, 4, 10, and 11) under appeal.

I. REAL PARTY IN INTEREST

Appellants have assigned the entire right and interest in the instant application to Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any other appeals or interferences which will directly affect, or be directly affected by, or having a bearing on the Board's decision in the present appeal.

III. STATUS OF CLAIMS

Original claims 1-4 of this application were elected for prosecution and non-elected claims 5-9 were withdrawn from consideration by the Examiner. Claim 2 was canceled without prejudice; claims 1, 3, and 4 were amended; and new claims 10 and 11[1] were added in an Amendment filed on April 11, 2001. Claims 1, 3, 4, and 10-11 have been finally rejected in an Office Action mailed July 3, 2001. Claims 1 and 11 were further amended in an Amendment filed on January 3, 2002. A Notice of Appeal was filed on January 3, 2002 appealing the rejection of claims 1, 3, 4, and 10-11.

IV. STATUS OF AMENDMENTS

Subsequent to the final rejection in the Office Action made final dated July 3, 2001, Appellants submitted an amendment under Rule 116 dated January 3, 2002 in an attempt to secure allowance of claims. The amendment has overcome certain rejection but fails to place the application in condition for allowance, as indicated in the Advisory Action from the Examiner mailed January 29, 2002. However, for the purpose of Appeal, the Examiner entered the amendment since it reduces the issues involved. The Appellants' Brief On Appeal is directed at claims 1, 3, 4, and 10-11. A copy of the claims involved in this Appeal is presented in the attached Exhibit A.

V. SUMMARY OF THE INVENTION

The present invention, as described and claimed, relates to oligonucleotides and polynucleotides that are disclosed as SEQ ID NOS: 9-18 in the Sequence Listing. These oligonucleotides and polynucleotides are discovered using gene trap technology in human teratocarcinoma cells.

According to the invention, the gene trap vectors used in the invention can integrate into intron sequences of cellular genes ("the trapped genes") in a genome and produce two fusion transcripts. See page 4, lines 19-24; page 75, lines 1-30; and Figures 1A to 1C. The first fusion transcript comprises the coding region of a selectable marker (neomycin resistance was used to produce the presently described oligonucleotides and polynucleotides) carried within the vector and the upstream exon(s) from the interrupted

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[1] New claims 5 and 6 filed on July 3, 2001 were renumbered as new claims 10 and 11 by the Examiner.

cellular gene. A mature transcript is generated when the splice donor (SD) and splice acceptor (SA) sites as shown in Figure 1C are spliced together. Translation of this transcript produces a fusion protein that allows for the selection of cells comprising an integrated gene trap vector. The second fusion transcript comprises exon 1 of the murine btk gene within the vector which is fused with exons of the trapped gene that are located downstream of the integration site. Unlike the first fusion transcript, transcription of this transcript is under the control of a vector-borne promoter (such as the PGK promoter), and the corresponding mRNA is generated by splicing between the splice donor (SD) and splice acceptor (SA) sites as shown in Figure 1B. To facilitate isolation of the trapped genes, cDNA was generated by reverse transcribing isolated RNA from pools of human teratocarcinoma cells that have undergone independent gene trap events. Based on the unique sequences present in the first exon of the murine btk gene, selective cloning of the fusion transcript is achieved as shown in Figure 1D and as described on page 76, line 1 to page 77, line 2.

Teratocarcinoma cells are the "stem cells" that occur in unusual germ cell tumors and represent a good model for molecular mechanisms of embryonic development and differentiation. These cells generate almost any kind of tissues such as teeth, hair, bone, muscle, and cartilage. Stem cells possess the ability both to produce identical daughter cells (self-renewal), and to produce progeny with more restricted fates (commitment and differentiation). This property of stem cells underpins growth and diversification during development and sustains homeostasis and repair processes throughout adult life. An understanding of molecular mechanisms which govern stem cell fate is therefore of fundamental significance in cell and developmental biology and the capabilities arising from such knowledge have major biomedical applications.

Example 6.1 (pages 74-80; Figures 1A-1D) demonstrated the identification of oligonucleotides and polynucleotides from human teratocarcinoma cells comprising the claimed nucleic acid sequences of SEQ ID NOS:9-18.

VI. ISSUES

The following issues are presented for review in this appeal:

A. UTILITY

(1) Whether claims 1, 3, 4, and 10-11 lack patentable utility under 35 U.S.C. § 101 for the lack of a specific, substantial, and credible utility. In the Office Actions dated October 12, 2000, July 3, 2001, and an advisory action dated January 29, 2002, the Examiner contended:

(a) that claims 1, 3, 4, and 10-11 are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid;

(b) that the claimed nucleic acid compounds are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter; and

(c) since the claimed invention is not supported by a specific and substantial asserted utility, credibility has not been assessed.

As discussed below, the Examiner's contentions are in error, and the rejection should be reversed.

(2) Whether claims 1, 3, 4, and 10-11 lack patentable utility under 35 U.S.C. § 112, first paragraph. In the Office Actions dated October 12, 2000 and July 3, 2001, the Examiner contended that since claims 1, 3, 4, and 10-11 are not supported by either a specific or substantial utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

As discussed below, the Examiner's contention is in error, and the rejection should be reversed.

B. WRITTEN DESCRIPTION

Whether claims 1, 3, 4, and 10-11 contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention under 35 U.S.C. § 112, second paragraph. In the Office Actions dated October 12, 2000 and July 3, 2001, the Examiner contended that while the specification discloses SEQ ID NOS: 9-18, the specification provides insufficient written description to support the genus of nucleotide sequences that comprise SEQ ID NOS: 9-18 or hybridizes to SEQ ID NOS: 9-18 which are encompassed by claims 1, 3, 4, and 10-12.

As discussed below, the Examiner's contention is in error, and the rejection should be reversed.

VII. GROUPING OF CLAIMS

A. UTILITY UNDER 35 U.S.C. § 101

Claims 1, 3, 4, and 10-11 stand rejected under 35 U.S.C. § 101 for the lack of a specific, substantial, and credible utility. Appellants believe that with regard to the issue of utility under 35 U.S.C. § 101, claims 1, 3, 4, and 10-11 stand or fall together.

B. UTILITY UNDER 35 U.S.C. § 112

Claims 1, 3, 4, and 10-11 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of utility. Appellants believe that with regard to the issue of utility under 35 U.S.C. § 112, first paragraph, claims 1, 3, 4, and 10-11 stand or fall together.

C. WRITTEN DESCRIPTION

Claims 1, 3, 4, and 10-11 stand rejected under 35 U.S.C. § 112, second paragraph, for lack of written description. Appellants believe that with regard to the issue of written description under 35 U.S.C. § 112, first paragraph, claims 1, 3, 4, and 10-11 stand or fall together.

VIII. ARGUMENTS

A. UTILITY OF THE REJECTED CLAIMS

Claims 1, 3, 4, and 10-11 are drawn to oligonucleotides or polynucleotides that comprise the nucleotide sequences of SEQ ID NOS: 9-18 or that hybridize to oligonucleotides or polynucleotides that comprise such nucleotide sequences. These claims have been rejected under 35 U.S.C. § 101.

According to 35 U.S.C. § 101, whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter may obtain a patent therefor subject to the conditions and requirements of 35 U.S.C. The threshold of utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). An invention is "useful" under 35 U.S.C. § 101 if it is capable of providing some identifiable benefit. *Id.* (*citing Brenner v. Manson*, 383 U.S. 519, 534, 148 USPQ 689, 695 (1966)).

Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)).

It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). The specification provides numerous specific, substantial, and credible utilities for the claimed nucleic acids comprising SEQ ID NOS:9-18. For instance, at page 8, lines 9-16, the specification describes the utility of polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18 for physical and genetic mapping of the human genome and/or the genome of model organisms. As explained in more detail below, the claimed nucleic acids can be used as probes, for example, in Northern blot analysis, or in situ hybridization, for different lineages or different stages of differentiation and development.

1. THE REJECTED CLAIMS HAVE SPECIFIC UTILITY

The Examiner has based the rejection of claims 1, 3, 4, and 10-11 on the contentions that the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid (*See* Office Action dated October 12, 2000, page 6, lines 2-4; and Office Action dated July 3, 2001, page 3, lines 18-20).

According to the Examination Guidelines for the Utility Requirement ("Examination Guidelines"), if the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.*, it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 FR 1098, Jan. 5, 2001).

> "A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record."

The definition of specific utility may be found in the Revised Interim Utility Guidelines Training Materials. Specific utility is:

> "a utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed." (Http://www/uspto.gov/web/menu/utility).

Unlike the example cited in the above definition where any fragment of genomic DNA can in theory be used as a probe or a chromosome marker, the polynucleotide sequences of SEQ ID NOS: 9-18 have utilities that are not common to any gene in the genome.

Appellants submit that contrary to the Examiner's contention, the polynucleotide sequences of SEQ ID NOS: 9-18 have specific utilities which stem from their cellular origin and the identification process. As explained in the Summary of The Invention hereinabove, gene trap vectors were introduced into human teratocarcinoma cells which led to the identification of gene loci that comprise the sequences set forth in SEQ ID NOS: 9-18. In particular, as the gene trap vector were introduced into the human teratocarcinoma cell, they integrated into the cell's genome resulting in gene fusions. Each fusion produces a transcript that comprises one or more exons that are located either upstream or downstream from the integration site. These exons, which are portions of a genetic locus that was disrupted by a gene trap vector, are represented by the presently claimed oligonucleotides and polynucleotides.

Appellants respectfully point out that the genetic loci in the teratocarcinoma cells which have been identified by the gene trap vectors fall within a specific class of genes which are distinct from the broad general class of genes in the genome. Apparently, these identified genetic loci encode genetic functions, the full complement of which are <u>not</u> critically essential to the survival and growth of teratocarcinoma cells. After transfection with the gene trap vectors, the teratocarcinoma cells survived and propagated in culture with

only one fully functional allele of the genetic loci. Thus, these genetic loci and the products encoded by these loci are preselected by the transfection and the ensuing cell culture process for possessing functions involved in later stages of cell differentiation and development. Appellants emphasize that the sequences set forth in SEQ ID Nos: 9-18 are not identified from the human genome randomly, rather, they represent a selection of genetic sequences that play a role in the later stages of cellular differentiation and development. Moreover, genes that are critically essential to the survival of teratocarcinoma cells would not have been isolated and propagated by the gene trap methods of the invention, as cells bearing disruptions in such a class of genes would not have been able to survive after transfection with the gene trap vector. Accordingly, the utility of these sequences are not general because not every gene in the genome, when disrupted, necessarily provide the specific utility of the oligonucleotides and polynucleotides of the invention.

After considering the above arguments presented in the amendment dated January 3, 2002, the Examiner stated in the advisory action dated January 29, 2002 that although "the claimed nucleic acids might be specific to the site of expression (or extraction), the claimed nucleic acids lack a substantial utility". The Examiner appears to contend that the claimed nucleic acids do not have specific utility because the nucleic acids lack a substantial utility. Appellants submit that the requirements for specific utility and substantial utility are separate and that the standards for specific utility and substantial utility are separate. As discussed above, specific utility is defined as a utility that is specific to the subject matter claimed. Appellants respectfully reiterate that the utility of the claimed nucleic acids in studying teratocarcinoma or stem cell development is <u>not</u> shared by every gene in the genome, and therefore a specific utility.

The utilities of the claimed oligonucleotides and polynucleotides are further discussed hereinbelow where it is shown that the utilities are substantial and credible.

2. THE REJECTED CLAIMS HAVE SUBSTANTIAL AND CREDIBLE UTILITY

Appellants submit that the specification provides numerous substantial and credible utilities for polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18.

Substantial utility is:

> "a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably

> confirm a "real world" context of use are not substantial utilities." (Http://www/uspto.gov/web/menu/utility)

In the context of the utilities that are specific to the claimed polynucleotides or oligonucleotides, the claimed oligonucleotides and polynucleotides can be used as probes to facilitate the analysis of genetic loci that play a role during embryonic development and cell differentiation. Appellants submit that the use of probes to investigate stages of embryonic development and cell differentiation constitutes an already identified "real world" context of use. As discussed earlier, since the genetic loci and the products encoded by these loci are preselected for the regulation in later stages of cell differentiation and development, the claimed oligonuceotides and polynucleotides can be used as probes in hybridization assays well known in the art to determine the activity at the genetic loci during development and differentiation of the teratocarcinomas (*See* for example, page 12, lines 8-24; page 32, line 13 to page 33, line 24).

Teratocarcinomas are totipotent, and as it is well known in the art, that they may differentiate into many different cell types (such as teeth, hair, bone, muscle and cartilage) along various pathways upon induction by certain signals. Each of these pathways may require expression of one or more genes that are disclosed in the specification as filed and represented by the presently claimed oligonucleotides and polynucleotides. Thus, the claimed oligonucleotides and polynucleotides can be used as probes, for example, in Northern blot analysis (page 41, line 6), or in situ hybridization (page 43, lines 21-29), for undifferentiated teratocarcinomas or differentiated teratocarcinomas of different lineages or at different stages of differentiation and development. The expression pattern of each of these genes can thus be correlated with known or observed events that occur in particular stages of development and cell differentiation. As such, the utility is substantial and credible in a real world context.

The polynucleotides or oligonucleotides of the invention can also be used for diagnostic gene expression and analysis, for cross species hybridization analysis, antisense inhibition, gene targeting, identifying exon splice junctions, gene therapy, gene delivery and chromosome mapping. *See*, for example, page 12, lines 8-12.

In the Office Action dated July 3, 2001, the Examiner contended that in order to have substantial utility, hybridization of a nucleic acid has to infer useful information. Appellants submit that these genetic loci as represented by the presently claimed nucleic

acids have substantial utility because they provide useful information regarding gene expression in teratocarcinoma cells which mimics gene expression during the late stages of stem cell differentiation and development.

After considering the above arguments presented in the amendment dated January 3, 2002, in the advisory action dated January 29, 2002, the Examiner contended that the claimed nucleic acids lack substantial utility because a skilled artisan would not know how to apply the results of the hybridization of the claimed nucleic acid for a real-world application. Appellants respectfully point out that the Examiner's comment is directed to a question of enablement and not that of substantial utility, and is thus misplaced. Specifically, the Examiner stated an example: "If a nucleic acid 'a' is expressed more, what does it mean?". Appellants submit that if the claimed nucleic acid detects an upregulation of nucleic acid 'a' in teratocarcinoma cells at a particular stage of differentiation and development, one of skilled in the art would infer that nucleic acid 'a' plays a role in the differentiation and development of the cells at that particular stage or in that lineage. Thus, Appellants reiterate that no further research is necessary to identify a "real world" context for utility and that investigation into differential gene expression during embryonic development and cell differentiation constitutes a "real world" context of use.

Furthermore, the gene trapped sequences of the present invention overcome some of the limitations of conventional cDNA and expressed sequence tag libraries. In particular, the claimed oligonucleotide and polynucleotide sequences were identified using gene trap vectors that do not rely solely on the level of endogenous mRNA expression of a gene for identification of that gene. The gene trap vectors are able to trap poorly expressed genes.

Appellants submit that the above described utilities are well known in the art, and hence utilities of the present invention are credible. As stated in the Examination Guidelines for the Utility Requirement, credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure or any other evidence of record (66 FR 1098, Jan 5, 2001). Accordingly, not only do the oligonucleotides and polynucleotides of the present invention have specific utilities, their utilities are credible and practical.

In view of the foregoing, Appellants submit that the claimed invention has specific, substantial and credible utility.

B. THE REJECTED CLAIMS HAVE UTILITY UNDER 35 U.S.C.§112, FIRST PARAGRAPH

Claims 1, 3, 4, 10, and 11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility.

The Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis – the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); *see also In re Jolles*, 628 F.2d 1322, 1326 n. 11, 206 USPQ 885, 889 n. 11 (CCPA 1980); and *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971).

Appellants traverse this rejection on the ground that Claims 1, 3, 4, 10, and 11 have significant patentable utility as discussed in Section A, above. Appellants submit that when an Appellant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn.

C. THE REJECTED CLAIMS AND THE SPECIFICATION MEET THE WRITTEN DESCRIPTION REQUIREMENT

Claims 1, 3, 4, 10, and 11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. The Examiner alleges that claims 1-4 are directed to gene sequences *comprising* and sequences that *hybridize* to SEQ ID NO: 9-18, and that only SEQ ID NO: 9-18 but not the full breadth of the claim meet the written description requirement. The Examiner contends that the species specifically disclosed are not representative of the genus because the genus is highly variant. The rejection is erroneous.

According to applicable case law, an applicant must convey with reasonably clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). "The written description must communicate that which is needed to enable the skilled artisan to make and use the claimed invention." *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419, 1421, 5 USPQ2d 1194, 1197 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988).

Claims 1, 3, 4, 10, and 11 recite synthetic oligonucleotides or isolated polynucleotides corresponding to one of SEQ ID NOS: 9-18. The synthetic oligonucleotides or isolated polynucleotides are fully described by *structure* or by *physical properties*, or both, sufficient to distinguish the claimed synthetic oligonucleotides or isolated polynucleotides from other materials. For instance, Claim 1 recites synthetic oligonucleotides that comprise a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS: 9-13, 15, 17, and 18. As the exact structure of SEQ ID NOS: 9-13, 15, 17, and 18 are provided in the specification, although there are numerous oligonucleotides that falls within this description, one person of skilled in the art can readily recognizes the synthetic oligonucleotide as described in claim 1. Likewise, claim 11 describes a genus of polynucleotides by a property (i.e., hybridizable under defined conditions to known sequences) that readily distinguishes the claimed polynucleotides from other materials. One of skill in the art can readily compare a polynucleotide with the claimed polynucleotides of Claim 11 by performing a hybridization as recited in the claim.

Appellants respectfully point out that the chemical structure of the claimed genus of nucleic acid molecules are described and well known in the art (e.g., DNA, RNA) and that the variation of nucleotide sequence within the claimed genus is also well defined by the functional characteristics of specifically binding under defined hybridizing conditions to nucleic acid molecules of known sequences. According to the Examination Guidelines Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement (66 FR 1099-1111, Jan. 5, 2001), the written description requirement may be satisfied by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See footnote 42 of the Examination Guidelines wherein it is stated that examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length, and also detailed restriction enzyme maps, antibody cross-reactivity, unique cleavage by particular enzymes. One of skill in the art would recognize from the combination of identifying structural and functional characteristics disclosed in the specification that Appellants have possession of the claimed genus of nucleic acid molecules. In fact, the skilled person can readily recognize and determine whether a nucleic acid molecule falls

within the pending claims by either comparing the sequence of the molecule with the sequences provided in the application and/or performing a hybridization reaction under defined conditions with the nucleic acid molecule(s) described in the present application. As such, Appellants submit that adequate written description has been provided.

After considering the arguments presented in the amendment dated January 3, 2002, in the advisory action dated January 29, 2002, the Examiner contended that the specification lacks written description of the claimed nucleic acids because the specification did not disclose the full open reading frame from which the oligonucleotides are derived.

The Examiner cited the Examination Guidelines Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement (66 FR 1099-1111, Jan. 5, 2001) ("Written Description Examination Guidelines"), which outlined the treatment of expressed sequence tags ("ESTs") during patent prosecution. Contrary to the example cited in the Written Description Examination Guidelines where the specification does not address whether the EST crosses an exon/intron splice junction and hence lacks information regarding the coding capacity of any ESTs, Appellants submit that the claimed nucleic acids are not ESTs. As discussed above, the claimed nucleic acids were isolated by gene trap vectors in which a corresponding mRNA is generated by splicing between the splice donor and splice acceptor sites as disclosed in the specification. Thus, the trapped genes of the invention always begin or end at the boundary of an exon/intron.

The Examiner also alleges that there is no description of other elements included in DNA, such as non-coding, regulatory regions, etc. Appellants submit that the term "comprising" is a term of art that is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. *See Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986), *cert. denied*, 479 U.S. 1030 (1987); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Pat. Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). The specification discloses exemplary elements that may be included in the claimed oligonucleotides or polynucleotides, such as non-coding or regulatory regions (page 23, lines 13-20); vector sequences (page 26, lines 15-19), other coding sequences as obtained by "primer extension" (page 10, lines 18-23). As such, the specification is replete with description of representative elements that may be included in the claimed oligonucleotides and polynucleotides.

IX. CONCLUSION

For the reasons set forth above, Appellants respectfully request that the rejection of the claims on appeal under 35 U.S.C. §§ 101 and 112 be reversed.

Respectfully submitted,

By: D Christiansen 40,258

Laura A. Coruzzi 30,742

Date: August 5, 2002

Laura A. Coruzzi (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosures

EXHIBIT A: APPENDIX TO APPELLANTS' BRIEF ON APPEAL

CLAIMS ON APPEAL
Serial No. 09/398,253
Attorney Docket No. 8535-026

1. (Twice Amended) An oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, and 18.

3. (Twice Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9-18.

4. (Twice Amended) The isolated polynucleotide according to Claim 3, wherein said polynucleotide sequence comprising at least one of SEQ ID NOS:9-18.

10. (Amended) A synthetic oligonucleotide comprising a contiguous stretch of at least about 20 nucleotides of at least one of SEQ ID NOS:16.

11. (Amended) An isolated polynucleotide capable of hybridizing to a polynucleotide or an oligonucleotide of Claim 1, 3, 4, or 5 under high stringency conditions comprising incubating at 65°C in 0.5M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1mM EDTA and washing at 68°C in 0.1xSSC and 0.1% SDS.